

SEQUENCE LISTING

<110> MILBURN, MICHAEL V.

<120> PDE5A CRYSTAL STRUCTURE AND USES

<130> 039363-1106

<140> 10/771,833

<141> 2004-02-03

<150> 60/485,627

<151> 2003-07-07

<150> 60/444,734

<151> 2003-02-03

<160> 31

<170> PatentIn Ver. 3.2

<210> 1

<211> 875

<212> PRT

<213> Homo sapiens

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Ala Thr Arg Glu Met Val Asn Ala Trp Phe Ala Glu Arg Val His Thr 50 60

Ile Pro Val Cys Lys Glu Gly Ile Arg Gly His Thr Glu Ser Cys Ser 65 70 75 80

Cys Pro Leu Gln Gln Ser Pro Arg Ala Asp Asn Ser Val Pro Gly Thr 85 90 95

Pro Thr Arg Lys Ile Ser Ala Ser Glu Phe Asp Arg Pro Leu Arg Pro 100 105 110

Ile Val Val Lys Asp Ser Glu Gly Thr Val Ser Phe Leu Ser Asp Ser 115 120 125

Glu Lys Lys Glu Gln Met Pro Leu Thr Pro Pro Arg Phe Asp His Asp 130 135 140

Glu Gly Asp Gln Cys Ser Arg Leu Leu Glu Leu Val Lys Asp Ile Ser 145 150 155 160 Ser His Leu Asp Val Thr Ala Leu Cys His Lys Ile Phe Leu His Ile 165 170 175

His Gly Leu Ile Ser Ala Asp Arg Tyr Ser Leu Phe Leu Val Cys Glu 180 185 190

Asp Ser Ser Asn Asp Lys Phe Leu Ile Ser Arg Leu Phe Asp Val Ala 195 200 205

Glu Gly Ser Thr Leu Glu Glu Val Ser Asn Asn Cys Ile Arg Leu Glu 210 215 220

Trp Asn Lys Gly Ile Val Gly His Val Ala Ala Leu Gly Glu Pro Leu 225 230 235 240

Asn Ile Lys Asp Ala Tyr Glu Asp Pro Arg Phe Asn Ala Glu Val Asp 245 250 255

Gln Ile Thr Gly Tyr Lys Thr Gln Ser Ile Leu Cys Met Pro Ile Lys 260 265 270

Asn His Arg Glu Glu Val Val Gly Val Ala Gln Ala Ile Asn Lys Lys 275 280 285

Ser Gly Asn Gly Gly Thr Phe Thr Glu Lys Asp Glu Lys Asp Phe Ala 290 295 300

Ala Tyr Leu Ala Phe Cys Gly Ile Val Leu His Asn Ala Gln Leu Tyr 305 310 315 320

Glu Thr Ser Leu Leu Glu Asn Lys Arg Asn Gln Val Leu Leu Asp Leu 325 330 335

Ala Ser Leu Ile Phe Glu Glu Gln Gln Ser Leu Glu Val Ile Leu Lys 340 345 350

Lys Ile Ala Ala Thr Ile Ile Ser Phe Met Gln Val Gln Lys Cys Thr 355 360 365

Ile Phe Ile Val Asp Glu Asp Cys Ser Asp Ser Phe Ser Ser Val Phe 370 380

His Met Glu Cys Glu Glu Leu Glu Lys Ser Ser Asp Thr Leu Thr Arg 385 390 395 400

Glu His Asp Ala Asn Lys Ile Asn Tyr Met Tyr Ala Gln Tyr Val Lys 405 410 415

Asn Thr Met Glu Pro Leu Asn Ile Pro Asp Val Ser Lys Asp Lys Arg
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Arg Ser Leu Leu Cys Thr Pro Ile Lys Asn Gly Lys Lys Asn Lys Val $_{450}$ $_{460}$

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Val Lys Pro Phe Asn Arg Asn Asp Glu Gln Phe Leu Glu Ala Phe Val
485 490 495

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Glu Arg Ala Met Ala Lys Gln Met Val Thr Leu Glu Val Leu Ser Tyr 515 520 525

His Ala Ser Ala Ala Glu Glu Glu Thr Arg Glu Leu Gln Ser Leu Ala 530 535 540

Ala Ala Val Val Pro Ser Ala Gln Thr Leu Lys Ile Thr Asp Phe Ser 545 550 555 560

Phe Ser Asp Phe Glu Leu Ser Asp Leu Glu Thr Ala Leu Cys Thr Ile 565 570 575

Arg Met Phe Thr Asp Leu Asn Leu Val Gln Asn Phe Gln Met Lys His 580 585 590

Glu Val Leu Cys Arg Trp Ile Leu Ser Val Lys Lys Asn Tyr Arg Lys 595 600 605

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Asn Val Ala Tyr His Asn Trp Arg His Ala Phe Asn Thr Ala Gln Cys 610 615 620

Met Phe Ala Ala Leu Lys Ala Gly Lys Ile Gln Asn Lys Leu Thr Asp 625 630 635 640

Leu Glu Ile Leu Ala Leu Leu Ile Ala Ala Leu Ser His Asp Leu Asp 645 650 655

His Arg Gly Val Asn Asn Ser Tyr Ile Gln Arg Ser Glu His Pro Leu 660 665 670

Ala Gln Leu Tyr Cys His Ser Ile Met Glu His His His Phe Asp Gln 675 680 685

Cys Leu Met Ile Leu Asn Ser Pro Gly Asn Gln Ile Leu Ser Gly Leu 690 695 700

Ser Ile Glu Glu Tyr Lys Thr Thr Leu Lys Ile Ile Lys Gln Ala Ile
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Leu Ala Thr Asp Leu Ala Leu Tyr Ile Lys Arg Arg Gly Glu Phe Phe 725 730 735

Glu Leu Ile Arg Lys Asn Gln Phe Asn Leu Glu Asp Pro His Gln Lys
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Glu Leu Phe Leu Ala Met Leu Met Thr Ala Cys Asp Leu Ser Ala Ile 755 760 765

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cat atg ggatccggaa ttcaaaggcc tacgtcgact agagcctgca gtctcgacca
                                                                  220
His Met
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tcatcatcat catcattaat aaaagggcga attccagcac actggcggcc gttactagtg 280
gatccggctg ctaacaaagc ccgaaaggaa gctgagttgg ctgctgccac cgctgagcaa 340
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<212> PRT

<213> Homo sapiens

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Asp Phe Ser Phe Ser Asp Phe Glu Leu Ser Asp Leu Glu Thr Ala Leu 50 55 60

Cys Thr Ile Arg Met Phe Thr Asp Leu Asn Leu Val Gln Asn Phe Gln 65 70 75 80

Met Lys His Glu Val Leu Cys Arg Trp Ile Leu Ser Val Lys Lys Asn 85 90 95

Tyr Arg Lys Asn Val Ala Tyr His Asn Trp Arg His Ala Phe Asn Thr 100 105 110

Ala Gln Cys Met Phe Ala Ala Leu Lys Ala Gly Lys Ile Gln Asn Lys 115 120 125

Leu Thr Asp Leu Glu Ile Leu Ala Leu Leu Ile Ala Ala Leu Ser His 130 135 140

Asp Leu Asp His Arg Gly Val Asn Asn Ser Tyr Ile Gln Arg Ser Glu 145 150 155 160

His Pro Leu Ala Gln Leu Tyr Cys His Ser Ile Met Glu His His His 165 170 175

Phe Asp Gln Cys Leu Met Ile Leu Asn Ser Pro Gly Asn Gln Ile Leu 180 185 190

Ser Gly Leu Ser Ile Glu Glu Tyr Lys Thr Thr Leu Lys Ile Ile Lys 195 200 205

Gln Ala Ile Leu Ala Thr Asp Leu Ala Leu Tyr Ile Lys Arg Arg Gly 210 220.

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His Gln Lys Glu Leu Phe Leu Ala Met Leu Met Thr Ala Cys Asp Leu 245 250 255

Ser Ala Ile Thr Lys Pro Trp Pro Ile Gln Gln Arg Ile Ala Glu Leu 260 265 270

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Glu Ala Leu Thr His Val Ser Glu Asp Cys Phe Pro Leu Asp Gly
Cys Arg Lys Asn Arg Gln Lys Trp Gln Ala Leu Ala Glu Gln Glu
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<213> Homo sapiens

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Met Tyr Ala Ile Phe Gln Glu Arg Asp Leu Leu Lys Thr Phe Arg Ile 50 55 60

Ser Ser Asp Thr Phe Ile Thr Tyr Met Met Thr Leu Glu Asp His Tyr 65 70 75 80

His Ser Asp Val Ala Tyr His Asn Ser Leu His Ala Ala Asp Val Ala 85 90 95

Gln Ser Thr His Val Leu Leu Ser Thr Pro Ala Leu Asp Ala Val Phe 100 105 110

Thr Asp Leu Glu Ile Leu Ala Ala Ile Phe Ala Ala Ile His Asp 115 120 125

Val Asp His Pro Gly Val Ser Asn Gln Phe Leu Ile Asn Thr Asn Ser 130 135 140

Glu Leu Ala Leu Met Tyr Asn Asp Glu Ser Val Leu Glu Asn His His 145 150 155 160

Leu Ala Val Gly Phe Lys Leu Leu Gln Glu Glu His Cys Asp Ile Phe 165 170 175

Met Asn Leu Thr Lys Lys Gln Arg Gln Thr Leu Arg Lys Met Val Ile 180 185 190

Asp Met Val Leu Ala Thr Asp Met Ser Lys His Met Ser Leu Leu Ala 195 200 205

Asp Leu Lys Thr Met Val Glu Thr Lys Lys Val Thr Ser Ser Gly Val 210 215 220

Leu Leu Leu Asp Asn Tyr Thr Asp Arg Ile Gln Val Leu Arg Asn Met 225 230 235 240

Val His Cys Ala Asp Leu Ser Asn Pro Thr Lys Ser Leu Glu Leu Tyr 245 250 255

Arg Gln Trp Thr Asp Arg Ile Met Glu Glu Phe Phe Gln Gln Gly Asp
260 265 270

Lys Glu Arg Glu Arg Gly Met Glu Ile Ser Pro Met Cys Asp Lys His 275 280 285

Thr Ala Ser Val Glu Lys Ser Gln Val Gly Phe Ile Asp Tyr Ile Val 290 295 300 His Pro Leu Trp Glu Thr Trp Ala Asp Leu Val Gln Pro Asp Ala Gln 305 310 315 320

Asp Ile Leu Asp Thr Leu Glu Asp Asn Arg Asn Trp Tyr Gln Ser Met 325 330 335

Ile Pro Gln Ser Pro 340

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<213> Homo sapiens

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Ala Gly Tyr Ser His Asn Arg Pro Leu Thr Cys Ile Met Tyr Ala Ile 35 40 45

Phe Gln Glu Arg Asp Leu Leu Lys Thr Phe Arg Ile Ser Ser Asp Thr 50 55 60

Phe Ile Thr Tyr Met Met Thr Leu Glu Asp His Tyr His Ser Asp Val 65 70 75 80

Ala Tyr His Asn Ser Leu His Ala Ala Asp Val Ala Gln Ser Thr His 85 90 95

Val Leu Ser Thr Pro Ala Leu Asp Ala Val Phe Thr Asp Leu Glu
100 105 110

Ile Leu Ala Ala Ile Phe Ala Ala Ile His Asp Val Asp His Pro 115 120 125

Gly Val Ser Asn Gln Phe Leu Ile Asn Thr Asn Ser Glu Leu Ala Leu 130 135 140

Met Tyr Asn Asp Glu Ser Val Leu Glu Asn His His Leu Ala Val Gly 145 150 155 160

Phe Lys Leu Gln Glu Glu His Cys Asp Ile Phe Met Asn Leu Thr

Lys Lys Gln Arg Gln Thr Leu Arg Lys Met Val Ile Asp Met Val Leu 180 185 190

Ala Thr Asp Met Ser Lys His Met Ser Leu Leu Ala Asp Leu Lys Thr 195 200 205 Met Val Glu Thr Lys Lys Val Thr Ser Ser Gly Val Leu Leu Leu Asp 210 215 220

Asn Tyr Thr Asp Arg Ile Gln Val Leu Arg Asn Met Val His Cys Ala 225 230 235 240

Asp Leu Ser Asn Pro Thr Lys Ser Leu Glu Leu Tyr Arg Gln Trp Thr 245 250 255

Asp Arg Ile Met Glu Glu Phe Phe Gln Gln Gly Asp Lys Glu Arg Glu 260 265 270

Arg Gly Met Glu Ile Ser Pro Met Cys Asp Lys His Thr Ala Ser Val 275 280 285

Glu Lys Ser Gln Val Gly Phe Ile Asp Tyr Ile Val His Pro Leu Trp 290 295 300

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Pro

<210> 12

<211> 341

<212> PRT

<213> Homo sapiens

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Val Phe Arg Ile Ala Glu Leu Ser Gly Asn Arg Pro Leu Thr Val Ile 35 40 45

Met His Thr Ile Phe Gln Glu Arg Asp Leu Leu Lys Thr Phe Lys Ile 50 60

Pro Val Asp Thr Leu Ile Thr Tyr Leu Met Thr Leu Glu Asp His Tyr 65 70 75 80

His Ala Asp Val Ala Tyr His Asn Asn Ile His Ala Ala Asp Val Val 85 90 95

Gln Ser Thr His Val Leu Leu Ser Thr Pro Ala Leu Glu Ala Val Phe 100 105 110

Thr Asp Leu Glu Ile Leu Ala Ala Ile Phe Ala Ser Ala Ile His Asp 115 120 125 Val Asp His Pro Gly Val Ser Asn Gln Phe Leu Ile Asn Thr Asn Ser 130 135 140

Glu Leu Ala Leu Met Tyr Asn Asp Ser Ser Val Leu Glu Asn His His 145 150 155 160

Leu Ala Val Gly Phe Lys Leu Leu Gln Glu Glu Asn Cys Asp Ile Phe 165 170 175

Gln Asn Leu Thr Lys Lys Gln Arg Gln Ser Leu Arg Lys Met Val Ile 180 185 190

Asp Ile Val Leu Ala Thr Asp Met Ser Lys His Met Asn Leu Leu Ala 195 200 205

Asp Leu Lys Thr Met Val Glu Thr Lys Lys Val Thr Ser Ser Gly Val 210 215 220

Leu Leu Leu Asp Asn Tyr Ser Asp Arg Ile Gln Val Leu Gln Asn Met 225 230 230 240

Val His Cys Ala Asp Leu Ser Asn Pro Thr Lys Pro Leu Gln Leu Tyr 245 250 255

Arg Gln Trp Thr Asp Arg Ile Met Glu Glu Phe Phe Pro Gln Gly Asp
260 265 270

Arg Glu Arg Glu Arg Gly Met Glu Ile Ser Pro Met Cys Asp Lys His 275 280 285

Asn Ala Ser Val Glu Lys Ser Gln Val Gly Phe Ile Asp Tyr Ile Val 290 295 300

His Pro Leu Trp Glu Thr Trp Ala Asp Leu Val His Pro Asp Ala Gln 305 310 315 320

Asp Ile Leu Asp Thr Leu Glu Asp Asn Arg Glu Trp Tyr Gln Ser Thr 325 330 335

Ile Pro Gln Ser Pro 340

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- Ile Phe Cys Val Ser Asp Tyr Ala Gly Gly Arg Ser Leu Thr Cys Ile 35 40 45
- Met Tyr Met Ile Phe Gln Glu Arg Asp Leu Leu Lys Lys Phe Arg Ile 50 55 60
- Pro Val Asp Thr Met Val Thr Tyr Met Leu Thr Leu Glu Asp His Tyr 65 70 75 80
- His Ala Asp Val Ala Tyr His Asn Ser Leu His Ala Ala Asp Val Leu 85 90 95
- Gln Ser Thr His Val Leu Leu Ala Thr Pro Ala Leu Asp Ala Val Phe 100 105 110
- Thr Asp Leu Glu Ile Leu Ala Ala Leu Phe Ala Ala Ile His Asp 115 120 125
- Val Asp His Pro Gly Val Ser Asn Gln Phe Leu Ile Asn Thr Asn Ser 130 135 140
- Glu Leu Ala Leu Met Tyr Asn Asp Glu Ser Val Leu Glu Asn His His 145 150 155 160
- Leu Ala Val Gly Phe Lys Leu Leu Gln Glu Asp Asn Cys Asp Ile Phe 165 170 175
- Gln Asn Leu Ser Lys Arg Gln Arg Gln Ser Leu Arg Lys Met Val Ile 180 185 190
- Asp Met Val Leu Ala Thr Asp Met Ser Lys His Met Thr Leu Leu Ala 195 200 205
- Asp Leu Lys Thr Met Val Glu Thr Lys Lys Val Thr Ser Ser Gly Val 210 215 220
- Leu Leu Leu Asp Asn Tyr Ser Asp Arg Ile Gln Val Leu Arg Asn Met 225 230 230 235 240
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- Arg Glu Arg Glu Arg Gly Met Glu Ile Ser Pro Met Cys Asp Lys His 275 280 285
- Thr Ala Ser Val Glu Lys Ser Gln Val Gly Phe Ile Asp Tyr Ile Val 290 295 300
- His Pro Leu Trp Glu Thr Trp Ala Asp Leu Val His Pro Asp Ala Gln 305 310 . 315 320
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Ile Arg Gln Ser Pro 340

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Val Phe Lys Val Ala Glu Leu Ser Gly Asn Arg Pro Leu Thr Ala Ile 35 40 45

Ile Phe Ser Ile Phe Gln Glu Arg Asp Leu Leu Lys Thr Phe Gln Ile
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Pro Ala Asp Thr Leu Ala Thr Tyr Leu Leu Met Leu Glu Gly His Tyr 65 70 75 80

His Ala Asn Val Ala Tyr His Asn Ser Leu His Ala Ala Asp Val Ala 85 90 95

Gln Ser Thr His Val Leu Leu Ala Thr Pro Ala Leu Glu Ala Val Phe 100 105 110

Thr Asp Leu Glu Ile Leu Ala Ala Leu Phe Ala Ser Ala Ile His Asp 115 120 125

Val Asp His Pro Gly Val Ser Asn Gln Phe Leu Ile Asn Thr Asn Ser 130 135 140

Asp Val Ala Leu Met Tyr Asn Asp Ala Ser Val Leu Glu Asn His His 145 150 155 160

Leu Ala Val Gly Phe Lys Leu Leu Gln Ala Glu Asn Cys Asp Ile Phe 165 170 175

Gln Asn Leu Ser Ala Lys Gln Arg Leu Ser Leu Arg Arg Met Val Ile 180 185 190

Asp Met Val Leu Ala Thr Asp Met Ser Lys His Met Asn Leu Leu Ala 195 200 205

Asp Leu Lys Thr Met Val Glu Thr Lys Lys Val Thr Ser Leu Gly Val 210 215 220

Leu Leu Leu Asp Asn Tyr Ser Asp Arg Ile Gln Val Leu Gln Asn Leu 225 230 235 240

Val His Cys Ala Asp Leu Ser Asn Pro Thr Lys Pro Leu Pro Leu Tyr 245 250 255 Arg Gln Trp Thr Asp Arg Ile Met Ala Glu Phe Phe Gln Gln Gly Asp
260 265 270

Arg Glu Arg Glu Ser Gly Leu Asp Ile Ser Pro Met Cys Asp Lys His 275 280 285

Thr Ala Ser Val Glu Lys Ser Gln Val Gly Phe Ile Asp Tyr Ile Ala 290 295 300

His Pro Leu Trp Glu Thr Trp Ala Asp Leu Val His Pro Asp Ala Gln 305 310 315 320

Asp Leu Leu Asp Thr Leu Glu Asp Asn Arg Glu Trp Tyr Gln Ser Lys 325 330 335

Ile Pro Arg Ser Pro 340

<210> 15

<211> 392

<212> PRT

<213> Homo sapiens

<400> 15

Glu Arg Met Tyr Arg Lys Thr Tyr His Met Val Gly Leu Ala Tyr Pro 1 5 10

Ala Ala Val Ile Val Thr Leu Lys Asp Val Asp Lys Trp Ser Phe Asp 20 25 30

Val Phe Ala Leu Asn Glu Ala Ser Gly Glu His Ser Leu Lys Phe Met 35 40 45

Ile Tyr Glu Leu Phe Thr Arg Tyr Asp Leu Ile Asn Arg Phe Lys Ile
50 55 60

Pro Val Ser Cys Leu Ile Thr Phe Ala Glu Ala Leu Glu Val Gly Tyr 65 70 75 80

Ser Lys Tyr Lys Asn Pro Tyr His Asn Leu Ile His Ala Ala Asp Val 85 90 95

Thr Gln Thr Val His Tyr Ile Met Leu His Thr Gly Ile Met His Trp 100 105 110

Leu Thr Glu Leu Glu Ile Leu Ala Met Val Phe Ala Ala Ile His 115 120 125

Asp Tyr Glu His Thr Gly Thr Thr Asn Asn Phe His Ile Gln Thr Arg 130 135 140

Ser Asp Val Ala Ile Leu Tyr Asn Asp Arg Ser Val Leu Glu Asn His 145 150 155 160 His Val Ser Ala Ala Tyr Arg Leu Met Gln Glu Glu Met Asn Ile 165 170 175

Leu Ile Asn Leu Ser Lys Asp Asp Trp Arg Asp Leu Arg Asn Leu Val 180 185 190

Ile Glu Met Val Leu Ser Thr Asp Met Ser Gly His Phe Gln Gln Ile 195 200 205

Lys Asn Ile Arg Asn Ser Leu Gln Gln Pro Glu Gly Ile Asp Arg Ala 210 215 220

Lys Thr Met Ser Leu Ile Leu His Ala Ala Asp Ile Ser His Pro Ala 225 230 235 240

Lys Ser Trp Lys Leu His Tyr Arg Trp Thr Met Ala Leu Met Glu Glu 245 250 255

Phe Phe Leu Gln Gly Asp Lys Glu Ala Glu Leu Gly Leu Pro Phe Ser 260 265 270

Pro Leu Cys Asp Arg Lys Ser Thr Met Val Ala Gln Ser Gln Ile Gly 275 280 285

Phe Ile Asp Phe Ile Val Glu Pro Thr Phe Ser Leu Leu Thr Asp Ser 290 295 300

Thr Glu Lys Ile Val Ile Pro Leu Ile Glu Glu Ala Ser Lys Ala Glu 305 310 315 320

Thr Ser Ser Tyr Val Ala Ser Ser Ser Thr Thr Ile Val Gly Leu His 325 330 335

Ile Ala Asp Ala Leu Arg Arg Ser Asn Thr Lys Gly Ser Met Ser Asp 340 345 350

Gly Ser Tyr Ser Pro Asp Tyr Ser Leu Ala Ala Val Asp Leu Lys Ser 355 360 365

Phe Lys Asn Asn Leu Val Asp Ile Ile Gln Gln Asn Lys Glu Arg Trp 370 375 380

Lys Glu Leu Ala Ala Gln Arg Ala 385 390

<210> 16

<211> 389

<212> PRT

<213> Homo sapiens

<400> 16

Glu Arg Met Tyr Arg Arg Thr Ser Asn Met Val Gly Leu Ser Tyr Pro

Pro Ala Val Ile Glu Ala Leu Lys Asp Val Asp Lys Trp Ser Phe Asp 20 25 30

- Val Phe Ser Leu Asn Glu Ala Ser Gly Asp His Ala Leu Lys Phe Ile 35 40 45
- Phe Tyr Glu Leu Leu Thr Arg Tyr Asp Leu Ile Ser Arg Phe Lys Ile 50 55 60
- Pro Ile Ser Ala Leu Val Ser Phe Val Glu Ala Leu Glu Val Gly Tyr 65 70 75 80
- Ser Lys His Lys Asn Pro Tyr His Asn Leu Met His Ala Ala Asp Val 85 90 95
- Thr Gln Thr Val His Tyr Leu Leu Tyr Lys Thr Gly Val Ala Asn Trp
 100 105 110
- Leu Thr Glu Leu Glu Ile Phe Ala Ile Ile Phe Ser Ala Ala Ile His 115 120 125
- Asp Tyr Glu His Thr Gly Thr Thr Asn Asn Phe His Ile Gln Thr Arg 130 135 140
- Ser Asp Pro Ala Ile Leu Tyr Asn Asp Arg Ser Val Leu Glu Asn His 145 150 155 160
- His Leu Ser Ala Ala Tyr Arg Leu Leu Gln Asp Asp Glu Glu Met Asn 165 170 175
- Ile Leu Ile Asn Leu Ser Lys Asp Asp Trp Arg Glu Phe Arg Thr Leu 180 185 190
- Val Ile Glu Met Val Met Ala Thr Asp Met Ser Cys His Phe Gln Gln 195 200 205
- Ile Lys Ala Met Lys Thr Ala Leu Gln Gln Pro Glu Ala Ile Glu Lys 210 215 220
- Pro Lys Ala Leu Ser Leu Met Leu His Thr Ala Asp Ile Ser His Pro 225 230 235 240
- Ala Lys Ala Trp Asp Leu His His Arg Trp Thr Met Ser Leu Leu Glu 245 250 255
- Glu Phe Phe Arg Gln Gly Asp Arg Glu Ala Glu Leu Gly Leu Pro Phe 260 265 270
- Ser Pro Leu Cys Asp Arg Lys Ser Thr Met Val Ala Gln Ser Gln Val 275 280 285
- Gly Phe Ile Asp Phe Ile Val Glu Pro Thr Phe Thr Val Leu Thr Asp 290 295 300
- Met Thr Glu Lys Ile Val Ser Pro Leu Ile Asp Glu Thr Ser Gln Thr 305 310 315 320
- Gly Gly Thr Gly Gln Arg Arg Ser Ser Leu Asn Ser Ile Ser Ser Ser 325 330 335

Asp Ala Lys Arg Ser Gly Val Lys Thr Ser Gly Ser Glu Gly Ser Ala 340 345 350

Pro Ile Asn Asn Ser Val Ile Ser Val Asp Tyr Lys Ser Phe Lys Ala 355 360 365

Thr Trp Thr Glu Val Val His Ile Asn Arg Glu Arg Trp Arg Ala Lys 370 375 380

Val Pro Lys Glu Glu 385

<210> 17

<211> 369

<212> PRT

<213> Homo sapiens

<400> 17

Glu Arg Met Phe Arg Arg Thr Tyr Thr Ser Val Gly Pro Thr Tyr Ser 1 10 15

Thr Ala Val Leu Asn Cys Leu Lys Asn Leu Asp Leu Trp Cys Phe Asp 20 25 30

Val Phe Ser Leu Asn Gln Ala Ala Asp Asp His Ala Leu Arg Thr Ile 35 40 45

Val Phe Glu Leu Leu Thr Arg His Asn Leu Ile Ser Arg Phe Lys Ile 50 55 60

Pro Thr Val Phe Leu Met Ser Phe Leu Asp Ala Leu Glu Thr Gly Tyr 65 70 75 80

Gly Lys Tyr Lys Asn Pro Tyr His Asn Gln Ile His Ala Ala Asp Val 85 90 95

Thr Gln Thr Val His Cys Phe Leu Leu Arg Thr Gly Met Val His Cys 100 105 110

Leu Ser Glu Ile Glu Leu Leu Ala Ile Ile Phe Ala Ala Ala Ile His 115 120 125

Asp Tyr Glu His Thr Gly Thr Thr Asn Ser Phe His Ile Gln Thr Lys 130 135 140

Ser Glu Cys Ala Ile Val Tyr Asn Asp Arg Ser Val Leu Glu Asn His 145 150 155 160

His Ile Ser Ser Val Phe Arg Leu Met Gln Asp Asp Glu Met Asn Ile 165 170 175

Phe Ile Asn Leu Thr Lys Asp Glu Phe Val Glu Leu Arg Ala Leu Val 180 185 190 Ile Glu Met Val Leu Ala Thr Asp Met Ser Cys His Phe Gln Gln Val 195 200 205

Lys Thr Met Lys Thr Ala Leu Gln Gln Leu Glu Arg Ile Asp Lys Pro 210 215 220

Lys Ala Leu Ser Leu Leu Leu His Ala Ala Asp Ile Ser His Pro Thr 225 230 235 240

Lys Gln Trp Leu Val His Ser Arg Trp Thr Lys Ala Leu Met Glu Glu 245 250 255

Phe Phe Arg Gln Gly Asp Lys Glu Ala Glu Leu Gly Leu Pro Phe Ser 260 265 270

Pro Leu Cys Asp Arg Thr Ser Thr Leu Val Ala Gln Ser Gln Ile Gly 275 280 285

Phe Ile Asp Phe Ile Val Glu Pro Thr Phe Ser Val Leu Thr Asp Val 290 295 300

Ala Glu Lys Ser Val Gln Pro Leu Ala Asp Glu Asp Ser Lys Ser Lys 305 310 315 320

Asn Gln Pro Ser Phe Gln Trp Arg Gln Pro Ser Leu Asp Val Glu Val 325 330 335

Gly Asp Pro Asn Pro Asp Val Val Ser Phe Arg Ser Thr Trp Val Lys 340 345 350

Arg Ile Gln Glu Asn Lys Gln Lys Trp Lys Glu Arg Ala Ala Ser Gly 355 360 365

Ile

<210> 18

<211> 430

<212> PRT

<213> Homo sapiens

<400> 18

Met Phe Leu Asp Lys Pro Ile Leu Ala Pro Glu Pro Leu Val Met Asp

Asn Leu Asp Ser Ile Met Glu Gln Leu Asn Thr Trp Asn Phe Pro Ile 20 25 30

Phe Asp Leu Val Glu Asn Ile Gly Arg Lys Cys Gly Arg Ile Leu Ser 35 40 45

Gln Val Ser Tyr Arg Leu Phe Glu Asp Met Gly Leu Phe Glu Ala Phe 50 55 60

Lys Ile Pro Ile Arg Glu Phe Met Asn Tyr Phe His Ala Leu Glu Ile 65 70 75 80

- Gly Tyr Arg Asp Ile Pro Tyr His Asn Arg Ile His Ala Thr Asp Val 85 90 95
- Leu His Ala Val Trp Tyr Leu Thr Thr Gln Pro Ile Pro Gly Leu Ser 100 105 110
- Thr Val Ile Asn Asp His Gly Ser Thr Ser Asp Ser Asp Ser Asp Ser 115 120 125
- Gly Phe Thr His Gly His Met Gly Tyr Val Phe Ser Lys Thr Tyr Asn 130 135 140
- Glu Leu Met Ala Leu Tyr Val Ala Ala Ala Met His Asp Tyr Asp His
 165 170 175
- Pro Gly Arg Thr Asn Ala Phe Leu Val Ala Thr Ser Ala Pro Gln Ala 180 185 190
- Val Leu Tyr Asn Asp Arg Ser Val Leu Glu Asn His His Ala Ala 195 200 205
- Ala Trp Asn Leu Phe Met Ser Arg Pro Glu Tyr Asn Phe Leu Ile Asn 210 215 220
- Leu Asp His Val Glu Phe Lys His Phe Arg Phe Leu Val Ile Glu Ala 225 230 235 240
- Ile Leu Ala Thr Asp Leu Lys Lys His Phe Asp Phe Val Ala Lys Phe 245 250 255
- Asn Gly Lys Val Asn Asp Asp Val Gly Ile Asp Trp Thr Asn Glu Asn 260 265 270
- Asp Arg Leu Leu Val Cys Gln Met Cys Ile Lys Leu Ala Asp Ile Asn 275 280 285
- Gly Pro Ala Lys Cys Lys Glu Leu His Leu Gln Trp Thr Asp Gly Ile 290 295 300
- Val Asn Glu Phe Tyr Glu Gln Gly Asp Glu Glu Ala Ser Leu Gly Leu 305 310 315 320
- Pro Ile Ser Pro Phe Met Asp Arg Ser Ala Pro Gln Leu Ala Asn Leu 325 330 335
- Gln Glu Ser Phe Ile Ser His Ile Val Gly Pro Leu Cys Asn Ser Tyr 340 345 350
- Asp Ser Ala Gly Leu Met Pro Gly Lys Trp Val Glu Asp Ser Asp Glu 355 360 365
- Ser Gly Asp Thr Asp Asp Pro Glu Glu Glu Glu Glu Glu Ala Pro Ala 370 375 380

Pro Asn Glu Glu Glu Thr Cys Glu Asn Asn Glu Ser Pro Lys Lys 385 390 395 400

Thr Phe Lys Arg Arg Lys Ile Tyr Cys Gln Ile Thr Gln His Leu Leu 405 410 415

Gln Asn His Lys Met Trp Lys Lys Val Ile Glu Glu Gln
420 425 430

<210> 19

<211> 432

<212> PRT

<213> Homo sapiens

<400> 19

Gln Gln Thr Asn Ile Glu Gln Glu Val Ser Leu Asp Leu Ile Leu Val 1 5 10 15

Glu Glu Tyr Asp Ser Leu Ile Glu Lys Met Ser Asn Trp Asn Phe Pro 20 25 30

Ile Phe Glu Leu Val Glu Lys Met Gly Glu Lys Ser Gly Arg Ile Leu $35 \hspace{1cm} 40 \hspace{1cm} 45$

Ser Gln Val Met Tyr Thr Leu Phe Gln Asp Thr Gly Leu Leu Glu Ile 50 55 60

Phe Lys Ile Pro Thr Gln Gln Phe Met Asn Tyr Phe Arg Ala Leu Glu 65 70 75 80

Asn Gly Tyr Arg Asp Ile Pro Tyr His Asn Arg Ile His Ala Thr Asp 85 90 95

Val Leu His Ala Val Trp Tyr Leu Thr Thr Arg Pro Val Pro Gly Leu 100 105 110

Gln Gln Ile His Asn Gly Cys Gly Thr Gly Asn Glu Thr Asp Ser Asp 115 120 125

Gly Arg Ile Asn His Gly Arg Ile Ala Tyr Ile Ser Ser Lys Ser Cys 130 135 140

Ser Asn Pro Asp Glu Ser Tyr Gly Cys Leu Ser Ser Asn Ile Pro Ala 145 150 155 160

Leu Glu Leu Met Ala Leu Tyr Val Ala Ala Ala Met His Asp Tyr Asp 165 170 175

His Pro Gly Arg Thr Asn Ala Phe Leu Val Ala Thr Asn Ala Pro Gln 180 185 190

Ala Val Leu Tyr Asn Asp Arg Ser Val Leu Glu Asn His His Ala Ala 195 200 205 Ser Ala Trp Asn Leu Tyr Leu Ser Arg Pro Glu Tyr Asn Phe Leu Leu 210 215 220

His Leu Asp His Val Glu Phe Lys Arg Phe Arg Phe Leu Val Ile Glu 225 230 235 240

Ala Ile Leu Ala Thr Asp Leu Lys Lys His Phe Asp Phe Leu Ala Glu 245 250 255

Phe Asn Ala Lys Ala Asn Asp Val Asn Ser Asn Gly Ile Glu Trp Ser 260 265 270

Asn Glu Asn Asp Arg Leu Leu Val Cys Gln Val Cys Ile Lys Leu Ala 275 280 285

Asp Ile Asn Gly Pro Ala Lys Val Arg Asp Leu His Leu Lys Trp Thr 290 295 300

Glu Gly Ile Val Asn Glu Phe Tyr Glu Gln Gly Asp Glu Glu Ala Asn 305 310 315 320

Leu Gly Leu Pro Ile Ser Pro Phe Met Asp Arg Ser Ser Pro Gln Leu 325 330 335

Ala Lys Leu Gln Glu Ser Phe Ile Thr His Ile Val Gly Pro Leu Cys 340 345 350

Asn Ser Tyr Asp Ala Ala Gly Leu Leu Pro Gly Gln Trp Leu Glu Ala 355 360 365

Glu Glu Asp Asn Asp Thr Glu Ser Gly Asp Asp Glu Asp Gly Glu Glu 370 375 380

Leu Asp Thr Glu Asp Glu Glu Met Glu Asn Asn Leu Asn Pro Lys Pro 385 390 395 400

Pro Arg Arg Lys Ser Arg Arg Ile Phe Cys Gln Leu Met His His 405 410 415

Leu Thr Glu Asn His Lys Ile Trp Lys Glu Ile Val Glu Glu Glu Glu 420 425 430

<210> 20

<211> 352

<212> PRT

<213> Homo sapiens

<400> 20

Met Val Ser Ser Asn Ile Ile Thr Pro Ile Ser Leu Asp Asp Val Pro 1 5 10 15

Pro Arg Ile Ala Arg Ala Met Glu Asn Glu Glu Tyr Trp Asp Phe Asp 20 25 30

- Ile Phe Glu Leu Glu Ala Ala Thr His Asn Arg Pro Leu Ile Tyr Leu 35 40 45
- Gly Leu Lys Met Phe Ala Arg Phe Gly Ile Cys Glu Phe Leu His Cys
 50 60
- Ser Glu Ser Thr Leu Arg Ser Trp Leu Gln Ile Ile Glu Ala Asn Tyr 65 70 75 80
- His Ser Ser Asn Pro Tyr His Asn Ser Thr His Ser Ala Asp Val Leu 85 90 95
- His Ala Thr Ala Tyr Phe Leu Ser Lys Glu Arg Ile Lys Glu Thr Leu
 100 105 110
- Asp Pro Ile Asp Glu Val Ala Ala Leu Ile Ala Ala Thr Ile His Asp 115 120 125
- Val Asp His Pro Gly Arg Thr Asn Ser Phe Leu Cys Asn Ala Gly Ser 130 135 140
- Glu Leu Ala Ile Leu Tyr Asn Asp Thr Ala Val Leu Glu Ser His His 145 150 155 160
- Ala Ala Leu Ala Phe Gln Leu Thr Thr Gly Asp Asp Lys Cys Asn Ile 165 170 175
- Phe Lys Asn Met Glu Arg Asn Asp Tyr Arg Thr Leu Arg Gln Gly Ile 180 185 190
- Ile Asp Met Val Leu Ala Thr Glu Met Thr Lys His Phe Glu His Val 195 200 205
- Asn Lys Phe Val Asn Ser Ile Asn Lys Pro Leu Ala Thr Leu Glu Glu 210 215 220
- Asn Gly Glu Thr Asp Lys Asn Gln Glu Val Ile Asn Thr Met Leu Arg 225 230 235 240
- Thr Pro Glu Asn Arg Thr Leu Ile Lys Arg Met Leu Ile Lys Cys Ala 245 250 255
- Asp Val Ser Asn Pro Cys Arg Pro Leu Gln Tyr Cys Ile Glu Trp Ala 260 265 270
- Ala Arg Ile Ser Glu Glu Tyr Phe Ser Gln Thr Asp Glu Glu Lys Gln 275 280 285
- Gln Gly Leu Pro Val Val Met Pro Val Phe Asp Arg Asn Thr Cys Ser 290 295 300
- Ile Pro Lys Ser Gln Ile Ser Phe Ile Asp Tyr Phe Ile Thr Asp Met 305 310 315 320
- Phe Asp Ala Trp Asp Ala Phe Val Asp Leu Pro Asp Leu Met Gln His 325 330 335

Leu Asp Asn Asn Phe Lys Tyr Trp Lys Gly Leu Asp Glu Met Lys Leu 340 345 350

<210> 21

<211> 341

<212> PRT

<213> Homo sapiens

<400> 21

Met Pro Ile Thr Ile Asn Asp Val Pro Pro Cys Ile Ser Gln Leu Leu 1 5 10 15

Asp Asn Glu Glu Ser Trp Asp Phe Asn Ile Phe Glu Leu Glu Ala Ile 20 25 30

Thr His Lys Arg Pro Leu Val Tyr Leu Gly Leu Lys Val Phe Ser Arg 35 40 45

Phe Gly Val Cys Glu Phe Leu Asn Cys Ser Glu Thr Thr Leu Arg Ala 50 55 60

Trp Phe Gln Val Ile Glu Ala Asn Tyr His Ser Ser Asn Ala Tyr His 65 70 75 80

Asn Ser Thr His Ala Ala Asp Val Leu His Ala Thr Ala Phe Phe Leu 85 90 95

Gly Lys Glu Arg Val Lys Gly Ser Leu Asp Gln Leu Asp Glu Val Ala 100 105 110

Ala Leu Ile Ala Ala Thr Val His Asp Val Asp His Pro Gly Arg Thr
115 120 125

Asn Ser Phe Leu Cys Asn Ala Gly Ser Glu Leu Ala Val Leu Tyr Asn 130 135 140

Asp Thr Ala Val Leu Glu Ser His His Thr Ala Leu Ala Phe Gln Leu 145 150 155 160

Thr Val Lys Asp Thr Lys Cys Asn Ile Phe Lys Asn Ile Asp Arg Asn 165 170 175

His Tyr Arg Thr Leu Arg Gln Ala Ile Ile Asp Met Val Leu Ala Thr 180 185 190

Glu Met Thr Lys His Phe Glu His Val Asn Lys Phe Val Asn Ser Ile 195 200 205

Asn Lys Pro Met Ala Ala Glu Ile Glu Gly Ser Asp Cys Glu Cys Asn 210 215 220

Pro Ala Gly Lys Asn Phe Pro Glu Asn Gln Ile Leu Ile Lys Arg Met 225 230 235 240

Met Ile Lys Cys Ala Asp Val Ala Asn Pro Cys Arg Pro Leu Asp Leu 245 250 255

Cys Ile Glu Trp Ala Gly Arg Ile Ser Glu Glu Tyr Phe Ala Gln Thr 260 265 270

Asp Glu Glu Lys Arg Gln Gly Leu Pro Val Val Met Pro Val Phe Asp 275 280 285

Arg Asn Thr Cys Ser Ile Pro Lys Ser Gln Ile Ser Phe Ile Asp Tyr 290 295 300

Phe Ile Thr Asp Met Phe Asp Ala Trp Asp Ala Phe Ala His Leu Pro 305 310 315 320

Ala Leu Met Gln His Leu Ala Asp Asn Tyr Lys His Trp Lys Thr Leu 325 330 335

Asp Asp Leu Glu Cys 340

<210> 22

<211> 334

<212> PRT

<213> Homo sapiens

<400> 22

Gly Thr Ala Val Ser Asn Ser Leu Asn Ile Leu Asp Asp Asp Tyr Asn 1 5 10 15

Gly Gln Ala Lys Cys Met Leu Glu Lys Val Gly Asn Trp Asn Phe Asp 20 25 30

Ile Phe Leu Phe Asp Arg Leu Thr Asn Gly Asn Ser Leu Val Ser Leu 35 40 45

Thr Phe His Leu Phe Ser Leu His Gly Leu Ile Glu Tyr Phe His Leu 50 55 60

Asp Met Met Lys Leu Arg Arg Phe Leu Val Met Ile Gln Glu Asp Tyr 65 70 75 80

His Ser Gln Asn Pro Tyr His Asn Ala Val His Ala Ala Asp Val Thr 85 90 95

Gln Ala Met His Cys Tyr Leu Lys Glu Pro Lys Leu Ala Asn Ser Val 100 105 110

Thr Pro Trp Asp Ile Leu Leu Ser Leu Ile Ala Ala Ala Thr His Asp 115 120 125

Leu Asp His Pro Gly Val Asn Gln Pro Phe Leu Ile Lys Thr Asn His 130 135 140

Tyr Leu Ala Thr Leu Tyr Lys Asn Thr Ser Val Leu Glu Asn His His 145 150 155 160

Trp Arg Ser Ala Val Gly Leu Leu Arg Glu Ser Gly Leu Phe Ser His
165 170 175

Leu Pro Leu Glu Ser Arg Gln Gln Met Glu Thr Gln Ile Gly Ala Leu 180 185 190

Ile Leu Ala Thr Asp Ile Ser Arg Gln Asn Glu Tyr Leu Ser Leu Phe 195 200 205

Arg Ser His Leu Asp Arg Gly Asp Leu Cys Leu Glu Asp Thr Arg His 210 215 220

Arg His Leu Val Leu Gln Met Ala Leu Lys Cys Ala Asp Ile Cys Asn 225 230 235 240

Pro Cys Arg Thr Trp Glu Leu Ser Lys Gln Trp Ser Glu Lys Val Thr 245 250 255

Glu Glu Phe Phe His Gln Gly Asp Ile Glu Lys Lys Tyr His Leu Gly
260 265 270

Val Ser Pro Leu Cys Asp Arg His Thr Glu Ser Ile Ala Asn Ile Gln 275 280 285

Ile Gly Phe Met Thr Tyr Leu Val Glu Pro Leu Phe Thr Glu Trp Ala 290 295 300

Arg Phe Ser Asn Thr Arg Leu Ser Gln Thr Met Leu Gly His Val Gly 305 310 315 320

Leu Asn Lys Ala Ser Trp Lys Gly Leu Gln Arg Glu Gln Ser 325 330

<210> 23

<211> 335

<212> PRT

<213> Homo sapiens

<400> 23

Gly Ile Ile Pro Gln Ala Pro Leu His Leu Leu Asp Glu Asp Tyr Leu 1 5 10 15

Gly Gln Ala Arg His Met Leu Ser Lys Val Gly Met Trp Asp Phe Asp 20 25 30

Ile Phe Leu Phe Asp Arg Leu Thr Asn Gly Asn Ser Leu Val Thr Leu
35 40 45

Leu Cys His Leu Phe Asn Thr His Gly Leu Ile His His Phe Lys Leu 50 55 60

Asp Met Val Thr Leu His Arg Phe Leu Val Met Val Gln Glu Asp Tyr 65 70 75 80

His Ser Gln Asn Pro Tyr His Asn Ala Val His Ala Ala Asp Val Thr 85 90 95

Gln Ala Met His Cys Tyr Leu Lys Glu Pro Lys Leu Ala Ser Phe Leu 100 105 110

Thr Pro Leu Asp Ile Met Leu Gly Leu Leu Ala Ala Ala His Asp 115 120 125

Val Asp His Pro Gly Val Asn Gln Pro Phe Leu Ile Lys Thr Asn His 130 135 140

His Leu Ala Asn Leu Tyr Gln Asn Met Ser Val Leu Glu Asn His His 145 150 155 160

Trp Arg Ser Thr Ile Gly Met Leu Arg Glu Ser Arg Leu Leu Ala His
165 170 175

Leu Pro Lys Glu Met Thr Gln Asp Ile Glu Gln Gln Leu Gly Ser Leu 180 185 190

Ile Leu Ala Thr Asp Ile Asn Arg Gln Asn Glu Phe Leu Thr Arg Leu 195 200 205

Lys Ala His Leu His Asn Lys Asp Leu Arg Leu Glu Asp Ala Gln Asp 210 215 220

Arg His Phe Met Leu Gln Ile Ala Leu Lys Cys Ala Asp Ile Cys Asn 225 230 235 240

Pro Cys Arg Ile Trp Glu Met Ser Lys Gln Trp Ser Glu Arg Val Cys 245 250 255

Glu Glu Phe Tyr Arg Gln Gly Glu Leu Glu Gln Lys Phe Glu Leu Glu 260 265 270

Ile Ser Pro Leu Cys Asn Gln Gln Lys Asp Ser Ile Pro Ser Ile Gln 275 280 285

Ile Gly Phe Met Ser Tyr Ile Val Glu Pro Leu Phe Arg Glu Trp Ala 290 295 300

His Phe Thr Gly Asn Ser Thr Leu Ser Glu Asn Met Leu Gly His Leu 305 310 315 320

Ala His Asn Lys Ala Gln Trp Lys Ser Leu Leu Pro Arg Gln His
. 325 330 335

<210> 24

<211> 336

<212> PRT

<213> Homo sapiens

- <400> 24
- Leu Ser Tyr His Ala Ser Ala Ala Glu Glu Glu Thr Arg Glu Leu Gln 1 5 10 15
- Ser Leu Ala Ala Ala Val Val Pro Ser Ala Gln Thr Leu Lys Ile Thr 20 25 30
- Asp Phe Ser Phe Ser Asp Phe Glu Leu Ser Asp Leu Glu Thr Ala Leu 35 40 45
- Cys Thr Ile Arg Met Phe Thr Asp Leu Asn Leu Val Gln Asn Phe Gln 50 60
- Met Lys His Glu Val Leu Cys Arg Trp Ile Leu Ser Val Lys Lys Asn 65 70 75 80
- Tyr Arg Lys Asn Val Ala Tyr His Asn Trp Arg His Ala Phe Asn Thr 85 90 95
- Ala Gl
n Cys Met Phe Ala Ala Leu Lys Ala Gly Lys Ile Gl
n Asn Lys 100 105 110
- Leu Thr Asp Leu Glu Ile Leu Ala Leu Leu Ile Ala Ala Leu Ser His
 115 120 125
- Asp Leu Asp His Arg Gly Val Asn Asn Ser Tyr Ile Gln Arg Ser Glu 130 135 140
- His Pro Leu Ala Gln Leu Tyr Cys His Ser Ile Met Glu His His His 145 150 155 160
- Phe Asp Gln Cys Leu Met Ile Leu Asn Ser Pro Gly Asn Gln Ile Leu 165 170 175
- Ser Gly Leu Ser Ile Glu Glu Tyr Lys Thr Thr Leu Lys Ile Ile Lys 180 185 190
- Gln Ala Ile Leu Ala Thr Asp Leu Ala Leu Tyr Ile Lys Arg Arg Gly
 195 200 205
- Glu Phe Phe Glu Leu Ile Arg Lys Asn Gln Phe Asn Leu Glu Asp Pro 210 215 220
- His Gln Lys Glu Leu Phe Leu Ala Met Leu Met Thr Ala Cys Asp Leu 225 230 235 240
- Ser Ala Ile Thr Lys Pro Trp Pro Ile Gln Gln Arg Ile Ala Glu Leu 245 250 255
- Val Ala Thr Glu Phe Phe Asp Gln Gly Asp Arg Glu Arg Lys Glu Leu 260 265 270
- Asn Ile Glu Pro Thr Asp Leu Met Asn Arg Glu Lys Lys Asn Lys Ile 275 280 285
- Pro Ser Met Gln Val Gly Phe Ile Asp Ala Ile Cys Leu Gln Leu Tyr 290 295 300

Glu Ala Leu Thr His Val Ser Glu Asp Cys Phe Pro Leu Leu Asp Gly 305 310 315 320

Cys Arg Lys Asn Arg Gln Lys Trp Gln Ala Leu Ala Glu Gln Glu 325 330 335

<210> 25

<211> 336

<212> PRT

<213> Homo sapiens

<400> 25

Leu Asp Val Leu Ser Tyr His Ala Thr Cys Ser Lys Ala Glu Val Asp 1 5 10 15

Lys Phe Lys Ala Ala As
n Ile Pro Leu Val Ser Glu Leu Ala Ile Asp $20 \hspace{1.5cm} 25 \hspace{1.5cm} 30$

Asp Ile His Phe Asp Asp Phe Ser Leu Asp Val Asp Ala Met Ile Thr 35 40 45

Ala Ala Leu Arg Met Phe Met Glu Leu Gly Met Val Gln Lys Phe Lys 50 55 60

Ile Asp Tyr Glu Thr Leu Cys Arg Trp Leu Leu Thr Val Arg Lys Asn 65 70 75 80

Tyr Arg Met Val Leu Tyr His Asn Trp Arg His Ala Phe Asn Val Cys 85 90 95

Gln Leu Met Phe Ala Met Leu Thr Thr Ala Gly Phe Gln Asp Ile Leu 100 105 110

Thr Glu Val Glu Ile Leu Ala Val Ile Val Gly Cys Leu Cys His Asp 115 120 125

Leu Asp His Arg Gly Thr Asn Asn Ala Phe Gln Ala Lys Ser Gly Ser 130 135 140

Ala Leu Ala Gln Leu Tyr Gly Thr Ser Ala Thr Leu Glu His His His 145 150 155 160

Phe Asn His Ala Val Met Ile Leu Gln Ser Glu Gly His Asn Ile Phe 165 170 175

Ala Asn Leu Ser Ser Lys Glu Tyr Ser Asp Leu Met Gln Leu Lys 180 185 190

Gln Ser Ile Leu Ala Thr Asp Leu Thr Leu Tyr Phe Glu Arg Arg Thr 195 200 205 Glu Phe Phe Glu Leu Val Ser Lys Gly Glu Tyr Asp Trp Asn Ile Lys 210 215 220

Asn His Arg Asp Ile Phe Arg Ser Met Leu Met Thr Ala Cys Asp Leu 225 230 235 240

Gly Ala Val Thr Lys Pro Trp Glu Ile Ser Arg Gln Val Ala Glu Leu 245 250 255

Val Thr Ser Glu Phe Phe Glu Gln Gly Asp Arg Glu Arg Leu Glu Leu 260 265 270

Lys Leu Thr Pro Ser Ala Ile Phe Asp Arg Asn Arg Lys Asp Glu Leu 275 280 285

Pro Arg Leu Gln Leu Glu Trp Ile Asp Ser Ile Cys Met Pro Leu Tyr 290 295 300

Gln Ala Leu Val Lys Val Asn Val Lys Leu Lys Pro Met Leu Asp Ser 305 310 315 320

Val Ala Thr Asn Arg Ser Lys Trp Glu Glu Leu His Gln Lys Arg Leu
325 330 335

<210> 26

<211> 329

<212> PRT

<213> Homo sapiens

<400> 26

Met Glu Lys Leu Ser Tyr His Ser Ile Cys Thr Ser Glu Glu Trp Gln
1 5 10 15

Gly Leu Met Gln Phe Thr Leu Pro Val Arg Leu Cys Lys Glu Ile Glu 20 25 30

Leu Phe His Phe Asp Ile Gly Pro Phe Glu Asn Met Trp Pro Gly Ile 35 40 45

Phe Val Tyr Met Val His Arg Ser Cys Gly Thr Ser Cys Phe Glu Leu
50 55 60

Glu Lys Leu Cys Arg Phe Ile Met Ser Val Lys Lys Asn Tyr Arg Arg 65 70 75 80

Val Pro Tyr His Asn Trp Lys His Ala Val Thr Val Ala His Cys Met 85 90 95

Tyr Ala Ile Leu Gln Asn Asn His Thr Leu Phe Thr Asp Leu Glu Arg 100 105 110

Lys Gly Leu Leu Ile Ala Cys Leu Cys His Asp Leu Asp His Arg Gly 115 120 125 Phe Ser Asn Ser Tyr Leu Gln Lys Phe Asp His Pro Leu Ala Ala Leu 130 135 140

Tyr Ser Thr Ser Thr Met Glu Gln His His Phe Ser Gln Thr Val Ser 145 150 155 160

Ile Leu Gln Leu Glu Gly His Asn Ile Phe Ser Thr Leu Ser Ser Ser 165 170 175

Glu Tyr Glu Gln Val Leu Glu Ile Ile Arg Lys Ala Ile Ile Ala Thr 180 185 190

Asp Leu Ala Leu Tyr Phe Gly Asn Arg Lys Gln Leu Glu Glu Met Tyr 195 200 205

Gln Thr Gly Ser Leu Asn Leu Asn Asn Gln Ser His Arg Asp Arg Val 210 215 220

Ile Gly Leu Met Met Thr Ala Cys Asp Leu Cys Ser Val Thr Lys Leu 225 230 235 235

Trp Pro Val Thr Lys Leu Thr Ala Asn Asp Ile Tyr Ala Glu Phe Trp 245 250 255

Ala Glu Gly Asp Glu Met Lys Lys Leu Gly Ile Gln Pro Ile Pro Met 260 265 270

Met Asp Arg Asp Lys Lys Asp Glu Val Pro Gln Gly Gln Leu Gly Phe 275 280 285

Tyr Asn Ala Val Ala Ile Pro Cys Tyr Thr Thr Leu Thr Gln Ile Leu 290 295 300

Pro Pro Thr Glu Pro Leu Leu Lys Ala Cys Arg Asp Asn Leu Ser Gln 305 310 315 320

Trp Glu Lys Val Ile Arg Gly Glu Glu 325

<210> 27

<211> 345

<212> PRT

<213> Homo sapiens

<400> 27

Glu Val Tyr Gly Lys Glu Pro Trp Glu Cys Glu Glu Glu Glu Leu Ala 1 5 10 15

Glu Ile Leu Gln Ala Glu Leu Pro Asp Ala Asp Lys Tyr Glu Ile Asn 20 25 30

Lys Phe His Phe Ser Asp Leu Pro Leu Thr Glu Leu Glu Leu Val Lys
35 40 45

- Cys Gly Ile Gln Met Tyr Tyr Glu Leu Lys Val Val Asp Lys Phe His 50 55 60
- Ile Pro Gln Glu Ala Leu Val Arg Phe Met Tyr Ser Leu Ser Lys Gly 65 70 75 80
- Tyr Arg Lys Ile Thr Tyr His Asn Trp Arg His Gly Phe Asn Val Gly
 85 90 95
- Gln Thr Met Phe Ser Leu Leu Val Thr Gly Lys Leu Lys Arg Tyr Phe 100 105 110
- Thr Asp Leu Glu Ala Leu Ala Met Val Thr Ala Ala Phe Cys His Asp 115 120 125
- Ile Asp His Arg Gly Thr Asn Asn Leu Tyr Gln Met Lys Ser Gln Asn 130 135 140
- Pro Leu Ala Lys Leu His Gly Ser Ser Ile Leu Glu Arg His His Leu 145 150 155 160
- Glu Phe Gly Lys Thr Leu Leu Arg Asp Glu Ser Leu Asn Ile Phe Gln 165 170 175
- Asn Leu Asn Arg Arg Gln His Glu His Ala Ile His Met Met Asp Ile 180 185 190
- Ala Ile Ile Ala Thr Asp Leu Ala Leu Tyr Phe Lys Lys Arg Thr Met 195 200 205
- Phe Gln Lys Ile Val Asp Gln Ser Lys Thr Tyr Glu Ser Glu Gln Glu 210 215 220
- Trp Thr Gln Tyr Met Met Leu Glu Gln Thr Arg Lys Glu Ile Val Met 225 230 235 240
- Ala Met Met Met Thr Ala Cys Asp Leu Ser Ala Ile Thr Lys Pro Trp 245 250 255
- Glu Val Gln Ser Gln Val Ala Leu Leu Val Ala Ala Glu Phe Trp Glu 260 265 270
- Gln Gly Asp Leu Glu Arg Thr Val Leu Gln Gln Asn Pro Ile Pro Met 275 280 285
- Met Asp Arg Asn Lys Ala Asp Glu Leu Pro Lys Leu Gln Val Gly Phe 290 295 300
- Ile Asp Phe Val Cys Thr Phe Val Tyr Lys Glu Phe Ser Arg Phe His 305 310 315 320
- Glu Glu Ile Thr Pro Met Leu Asp Gly Ile Thr Asn Asn Arg Lys Glu 325 330 335
- Trp Lys Ala Leu Ala Asp Glu Tyr Asp 340 345

<210> 28

<211> 345

<212> PRT

<213> Homo sapiens

<400> 28

Ala Arg Leu Gly Lys Glu Pro Ala Asp Cys Asp Glu Asp Glu Leu Gly
1 5 10 15

Glu Ile Leu Lys Glu Glu Leu Pro Gly Pro Thr Thr Phe Asp Ile Tyr 20 25 30

Glu Phe His Phe Ser Asp Leu Glu Cys Thr Glu Leu Asp Leu Val Lys
35 40 45

Cys Gly Ile Gln Met Tyr Tyr Glu Leu Gly Val Val Arg Lys Phe Gln 50 55 60

Ile Pro Gln Glu Val Leu Val Arg Phe Leu Phe Ser Ile Ser Lys Gly 65 70 75 80

Tyr Arg Arg Ile Thr Tyr His Asn Trp Arg His Gly Phe Asn Val Ala 85 90 95

Gln Thr Met Phe Thr Leu Leu Met Thr Gly Lys Leu Lys Ser Tyr Tyr
100 105 110

Thr Asp Leu Glu Ala Phe Ala Met Val Thr Ala Gly Leu Cys His Asp 115 120 125

Ile Asp His Arg Gly Thr Asn Asn Leu Tyr Gln Met Lys Ser Gln Asn 130 135 140

Glu Phe Gly Lys Phe Leu Leu Ser Glu Glu Thr Leu Asn Ile Tyr Gln 165 170 175

Asn Leu Asn Arg Arg Gln His Glu His Val Ile His Leu Met Asp Ile 180 185 190

Ala Ile Ile Ala Thr Asp Leu Ala Leu Tyr Phe Lys Lys Arg Ala Met 195 200 205

Phe Gln Lys Ile Val Asp Glu Ser Lys Asn Tyr Gln Asp Lys Lys Ser 210 215 220

Trp Val Glu Tyr Leu Ser Leu Glu Thr Thr Arg Lys Glu Ile Val Met 225 230 235 240

Ala Met Met Met Thr Ala Cys Asp Leu Ser Ala Ile Thr Lys Pro Trp
245 250 255

Glu Val Gln Ser Lys Val Ala Leu Leu Val Ala Ala Glu Phe Trp Glu 260 265 270

Gln Gly Asp Leu Glu Arg Thr Val Leu Asp Gln Gln Pro Ile Pro Met 275 280 285

Met Asp Arg Asn Lys Ala Ala Glu Leu Pro Lys Leu Gln Val Gly Phe 290 295 300

Ile Asp Phe Val Cys Thr Phe Val Tyr Lys Glu Phe Ser Arg Phe His 305 310 315 320

Glu Glu Ile Leu Pro Met Phe Asp Arg Leu Gln Asn Asn Arg Lys Glu 325 330 335

Trp Lys Ala Leu Ala Asp Glu Tyr Glu 340 345

<210> 29

<211> 345

<212> PRT

<213> Homo sapiens

<400> 29

Lys Leu Asn Val Asp Val Ile Asp Asp Cys Glu Glu Lys Gln Leu Val 1 5 10 15

Ala Ile Leu Lys Glu Asp Leu Pro Asp Pro Arg Ser Ala Glu Leu Tyr 20 25 30

Glu Phe Arg Phe Ser Asp Phe Pro Leu Thr Glu His Gly Leu Ile Lys 35 40 45

Cys Gly Ile Arg Leu Phe Phe Glu Ile Asn Val Val Glu Lys Phe Lys 50 55 60

Val Pro Val Glu Val Leu Thr Arg Trp Met Tyr Thr Val Arg Lys Gly
65 70 75 80

Tyr Arg Ala Val Thr Tyr His Asn Trp Gln His Gly Phe Asn Val Gly 85 90 95

Gln Thr Met Phe Thr Leu Leu Met Thr Gly Arg Leu Lys Lys Tyr Tyr
100 105 110

Thr Asp Leu Glu Ala Phe Ala Met Leu Ala Ala Ala Phe Cys His Asp 115 120 125

Ile Asp His Arg Gly Thr Asn Asn Leu Tyr Gln Met Lys Ser Thr Ser 130 135 140

Pro Leu Ala Arg Leu His Gly Ser Ser Ile Leu Glu Arg His His Leu 145 150 155 160

Glu Tyr Ser Lys Thr Leu Leu Gln Asp Glu Ser Leu Asn Ile Phe Gln 165 170 175 Asn Leu Asn Lys Arg Gln Phe Glu Thr Val Ile His Leu Phe Glu Val

Ala Ile Ile Ala Thr Asp Leu Ala Leu Tyr Phe Lys Lys Arg Thr Met 195 200 205

Phe Gln Lys Ile Val Asp Ala Cys Glu Gln Met Gln Thr Glu Glu Glu 210 215 220

Ala Ile Lys Tyr Val Thr Val Asp Pro Thr Lys Lys Glu Ile Ile Met 225 230 235 240

Ala Met Met Met Thr Ala Cys Asp Leu Ser Ala Ile Thr Lys Pro Trp
245 250 255

Glu Val Gln Ser Gln Val Ala Leu Met Val Ala Asn Glu Phe Trp Glu 260 265 270

Gln Gly Asp Leu Glu Arg Thr Val Leu Gln Gln Gln Pro Ile Pro Met 275 280 285

Met Asp Arg Asn Lys Arg Asp Glu Leu Pro Lys Leu Gln Val Gly Phe 290 295 300

Ile Asp Phe Val Cys Thr Phe Val Tyr Lys Glu Phe Ser Arg Phe His 305 310 315 320

Lys Glu Ile Thr Pro Met Leu Ser Gly Leu Gln Asn Asn Arg Val Glu 325 330 335

Trp Lys Ser Leu Ala Asp Glu Tyr Asp 340 345

<210> 30

<211> 334

<212> PRT

<213> Homo sapiens

<400> 30

Met Met Met Tyr His Met Lys Val Ser Asp Asp Glu Tyr Thr Lys Leu 1 5 10 15

Leu His Asp Gly Ile Gln Pro Val Ala Ala Ile Asp Ser Asn Phe Ala 20 25 30

Ser Phe Thr Tyr Thr Pro Arg Ser Leu Pro Glu Asp Asp Thr Ser Met 35 40 45

Ala Ile Leu Ser Met Leu Gln Asp Met Asn Phe Ile Asn Asn Tyr Lys 50 55 60

Ile Asp Cys Pro Thr Leu Ala Arg Phe Cys Leu Met Val Lys Lys Gly 65 70 75 80

Tyr Arg Asp Pro Pro Tyr His Asn Trp Met His Ala Phe Ser Val Ser 85 90 95 His Phe Cys Tyr Leu Leu Tyr Lys Asn Leu Glu Leu Thr Asn Tyr Leu 100 105 110

Glu Asp Ile Glu Ile Phe Ala Leu Phe Ile Ser Cys Met Cys His Asp 115 120 125

Leu Asp His Arg Gly Thr Asn Asn Ser Phe Gln Val Ala Ser Lys Ser 130 135 140

Val Leu Ala Ala Leu Tyr Ser Ser Glu Gly Ser Val Met Glu Arg His 145 150 155 160

His Phe Ala Gln Ala Ile Ala Ile Leu Asn Thr His Gly Cys Asn Ile 165 170 175

Phe Asp His Phe Ser Arg Lys Asp Tyr Gln Arg Met Leu Asp Leu Met 180 185 190

Arg Asp Ile Ile Leu Ala Thr Asp Leu Ala His His Leu Arg Ile Phe 195 200 205

Lys Asp Leu Gln Lys Met Ala Glu Val Gly Tyr Asp Arg Asn Asn Lys 210 215 220

Gln His His Arg Leu Leu Cys Leu Leu Met Thr Ser Cys Asp Leu 225 230 235 240

Ser Asp Gln Thr Lys Gly Trp Lys Thr Thr Arg Lys Ile Ala Glu Leu 245 250 255

Ile Tyr Lys Glu Phe Phe Ser Gln Gly Asp Leu Glu Lys Ala Met Gly 260 265 270

Asn Arg Pro Met Glu Met Met Asp Arg Glu Lys Ala Tyr Ile Pro Glu 275 280 285

Leu Gln Ile Ser Phe Met Glu His Ile Ala Met Pro Ile Tyr Lys Leu 290 295 300

Leu Gln Asp Leu Phe Pro Lys Ala Ala Glu Leu Tyr Glu Arg Val Ala 305 310 315 320

Ser Asn Arg Glu His Trp Thr Lys Val Ser His Lys Phe Thr 325 330

<210> 31

<211> 333

<212> PRT

<213> Homo sapiens

<400> 31

Ser Phe Leu Asp Asn His Lys Lys Leu Thr Pro Arg Arg Asp Val Pro 1 5 10 15

- Thr Tyr Pro Lys Tyr Leu Leu Ser Pro Glu Thr Ile Glu Ala Leu Arg 20 25 30
- Lys Pro Thr Phe Asp Val Trp Leu Trp Glu Pro Asn Glu Met Leu Ser
- Cys Leu Glu His Met Tyr His Asp Leu Gly Leu Val Arg Asp Phe Ser 50 60
- Ile Asn Pro Val Thr Leu Arg Arg Trp Leu Phe Cys Val His Asp Asn 65 70 75 80
- Tyr Arg Asn Asn Pro Phe His Asn Phe Arg His Cys Phe Cys Val Ala 85 90 95
- Gln Met Met Tyr Ser Met Val Trp Leu Cys Ser Leu Gln Glu Lys Phe 100 105 110
- Ser Gln Thr Asp Ile Leu Ile Leu Met Thr Ala Ala Ile Cys His Asp 115 120 125
- Leu Asp His Pro Gly Tyr Asn Asn Thr Tyr Gln Ile Asn Ala Arg Thr 130 135 140
- Glu Leu Ala Val Arg Tyr Asn Asp Ile Ser Pro Leu Glu Asn His His 145 150 155 160
- Cys Ala Val Ala Phe Gln Ile Leu Ala Glu Pro Glu Cys Asn Ile Phe 165 170 175
- Ser Asn Ile Pro Pro Asp Gly Phe Lys Gln Ile Arg Gln Gly Met Ile 180 185 190
- Thr Leu Ile Leu Ala Thr Asp Met Ala Arg His Ala Glu Ile Met Asp 195 200 205
- Ser Phe Lys Glu Lys Met Glu Asn Phe Asp Tyr Ser Asn Glu Glu His 210 220
- Met Thr Leu Leu Lys Met Ile Leu Ile Lys Cys Cys Asp Ile Ser Asn 225 230 235 240
- Glu Val Arg Pro Met Glu Val Ala Glu Pro Trp Val Asp Cys Leu Leu 245 250 255
- Glu Glu Tyr Phe Met Gln Ser Asp Arg Glu Lys Ser Glu Gly Leu Pro 260 265 270
- Val Ala Pro Phe Met Asp Arg Asp Lys Val Thr Lys Ala Thr Ala Gln 275 280 285
- Ile Gly Phe Ile Lys Phe Val Leu Ile Pro Met Phe Glu Thr Val Thr 290 295 300
- Lys Leu Phe Pro Met Val Glu Glu Ile Met Leu Gln Pro Leu Trp Glu 305 310 315 320

Ser Arg Asp Arg Tyr Glu Glu Leu Lys Arg Ile Asp Asp 325 330